

Remarks

The following remarks are point-by-point response to Examiner's Objections/Rejections.

The original Objections/Rejections are shown here in *italic*.

Remark 1.

In Outstanding Objection(s) and/or Rejection(s), Claims 54-56 are rejected under 35USC 102(e) as being anticipated by Sabatini US Pat. No. 6,544,790.

In response, Claims 54-56 are now withdrawn.

Remark 2.

In New Objection(s) and/or Rejection(s), Claims 37-39, 43-46, 49 and 53-56 are rejected under 35 U.S.C. 112. The claims contain subject matter which was not described in the specification in such as way as to reasonable convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

A. In claims 37, 53 and 54 (and claims dependent thereon), the term "providing one or more said biological targets on a target support"; "biological target immobilized on said target support", "target support" and "separating said target support from said array"; to the extent that the "support" (which is broadly defined for immobilizing the reagent) is

broader than “growth support” the increase in breadth beyond growth support constitutes new matter. Additionally, separating “targeting supports” from the array is not described. In applicant’s amendment, applicant has failed to indicate where said support exists.

In response, Claims 37 and 53 are amended: “cell growth support” is used instead of “target support”. “Cell growth support” is clearly defined and used in the description (e.g. paragraph 0072).

Separating “cell growth support” from the array is described (see paragraph 0078).

Claim 54 is withdrawn.

B. In claims 37, 53 and 54 (and claims dependent thereon), the phrase “applying one or more conditions” to the extent that this term is broader than “applying one or more conditions to one or more of said reagent portions to facilitate...transfer...reagent portions...to corresponding target” the increase in breadth constitutes new matter. In other words the application of one or more conditions is limited to its specifically described purpose (e.g. as described and originally claimed e.g. see original claim 48). In applicant’s amendment, applicant has failed to indicate where said support exists.

In response, Claim 37 is amended as suggested by the Examiner to narrow the claim. The currently amended Claim 37 reads as:

“A method for bringing two or more reagents in contact with one or more biological targets comprising the steps of,

.....

applying one or more conditions to one or more of said reagent portions to facilitate said transfer of some or all of each specific reagent portion to said specific reagent portion's corresponding biological target”.

This step is described in many places in the specification, e.g. paragraph 0075-0077 and Example 3.

C. In claims 37, 53 and 54 (and claims dependent thereon), the phrase “...dissociates from said barriers...” does not find specification or original claim support. In fact, the specification indicates (e.g. in not-transfection embodiments) that covalent or strong non-covalent reagent immobilization is desirable (e.g. see bottom of specification page 20 to page 21). In this regard, the claim is not limited to DNA or Transfection, but reads on any reagent or assay embodiment.

In response, Claims are amended: “dissociates from said barriers” is used in the claim in stead of “....dissociates from said array...”.

The dissociation of reagents from the arrays is described in the specification (e.g., in Paragraphs 0076 and 0077).

Covalent or strong non-covalent reagent immobilization is described in the specification for making arrays. They are related to claims 22-36, which are now withdrawn.

Remark 3.

Claims 37, 43-46 and 53-55 are rejected under 35 USC 102 as being anticipated by Palsson US Pat. 5,811,274.

Palsson teaches a method of contacting 2 or more reagents with 1 or more biological targets comprising:

- a. providing an array or 2 or more reagents (e.g. "particles"; see col. 4 and patent claims) on a coated (e.g. polylysine) or uncoated "support" (e.g. cell growth support: see col. 5, especially lines 38- including membranes i.e. porous)...*
- b. providing 1 or more biological targets (e.g. eukaryotic cells: see col. 5) for contacting the reagent array in which the "biological targets" can be "localized" for contacting and/or immobilized (e.g. attached) to a support (e.g. see col. 3, especially lines 30-40);*
- c and d. applying 1 or more "conditions" to promote contact, dissociation and transfer (e.g. transfection) (e.g. see bottom of col. 7-col. 8) of the particle DNA into the cell(s) into the corresponding target cell(s). See also example and patent claims.*

The reference provides for the separation of the reagent array from the target.

The reference examples illustrate the monitoring of transfection efficiency through assays requiring the designation and corresponding of array locations spacially for both the reference reagent and target (if immobilized).

In response, the Applicant respectfully traverses the Examiner's conclusion and offers the following remarks.

a). Palsson did not describe the method of providing an array of 2 or more reagents. The reference teaches the immobilization of particles on a support without providing the positional information of the particles. The particles are treated as one reagent.

b). In the method of Palsson, the targets are provided onto the same support as the reagents. In contrast, in the method of Claim 37 and dependent claims, the reagents are provided on an array while the targets are provided on a separate cell growth support.

c). In addition, the present method (Claim 53) further comprises the step of separating said target support from said array. This step is not taught by the Palsson reference. In fact, since in the Palsson method, the cell targets are provided onto the same support as the reagents, it is impossible to separate said targets from the reagents.

Remark 4.

Claims 37, 43-46, 49 and 53-55 are rejected as being unpatentable over Palsson US Pat. 5,811,274 in view of Sabatini US Pat. No. 6,544,790.

“The Palsson reference teaching differs from the presently claimed invention by failing to teach applying electric impulses (e.g. electroporation) to the reagent as one of the conditions (e.g. present claims 49 and 56)”.

“Electroporation is a conventional means of promoting transfection as illustrated by the Sabatini reference (e.g. see col. 1, especially lines 30-40)”.

“Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant’s invention to modify the Palsson reference (see Palson at col. 8: which incorporated “standard” transfection condtions) in order to further promote transfection efficiency”.

In response, the Applicant respectfully traverses the Examiner’s conclusion and offers the following remarks.

Electroporation is cited in the Sabatini reference as a standard transfection method (col. 1 lines 30-40: “...a variety of DNA transfection methods, such as calcium phosphate coprecipitation, electroporation and cationic liposome-mediated transfection (e.g., lipofection) can be used to introduce DNA into cells and are useful in studying gene regulation and function....”).

However, standard electroporation is done with reagents and targets in solution (or in suspension). In the Palsson method, immobilized reagents are transfected into targets. There is no prior art that suggests using electroporation to transfect immobilized reagents into target cells. In fact, common sense indicates that electroporation will perform poorly in introducing immobilized reagents into target cells.

It is difficult if not impossible to use electroporation in the Palsson method. You would have to modify the Palsson method in several significant ways in order to use electroporation. First, the reagent support would have to be electricity conducive, a requirement for electroporation. Second, a setup would have to be established to connect the target cells and reagents to two electrodes (positive and negative ends of the power supply). These modifications are not taught or suggested in the Palsson or the Sabatini methods.

Furthermore, in the method of Claim 37, immobilized reagents are transfected into immobilized target cells. No prior art used or suggested the use of electroporation to transfect immobilized reagents into immobilized targets.

In addition, the Palsson reference teaching differs from the presently claimed invention in several other significant ways besides electroporation (see Remark 3). The Palsson reference (or Sabatini reference) does not teach the use of a reagent array while targets are on a cell growth support, as taught by the method of Claim 37. The cell growth

support is not the reagent array. The method of claim 53 further comprises the step of separating said target support from said array. These differences are not obvious in view of Sabatini.

Remark 5.

Claims 37, 43-46, 49 and 53-55 are rejected as being unpatentable over Sabatini US Pat. No. 6,544,790 in view of Palsson US Pat. 5,811,274 and/or Lockett et al. US Pat. No. 5,854,224.

“Sabatini teaches both a method and apparatus Following transfection, the slide may be removed for further processing (e.g. “separating target support from said array” claim 53). See e.g. examples”.

“The Sabatini reference differs from the presently claimed invention by plating the “target” cell directly onto the “reagent” (array) without the use of a “target” support”.

The Applicant respectfully disagrees with the Office Action’s interpretation of the Sabatini method that *“Following transfection, the slide may be removed for further processing (e.g. “separating target support from said array” claim 53). See e.g. examples”*. The removal of slide for further processing in the Sabatini method does not constitute separation of target from array. In the Sabatini reference, both the target and array are on the same slide: reagents (DNA) are arrayed on the slide and target cells are

seeded on the same slide. Therefore, the target and the array cannot be separated in Sabatini method.

The method of Claim 53 comprises the step of separating said target support from said array. This is not taught by the Sabatini method. This step is not taught in the Palsson or the Lockett et al method. Therefore, the method of Claim 53 is not obvious over Sabatini in view of Palsson and/or Lockett et al.

“However, the Lockett reference teaches a transfection method (e.g. see TRANSFECTION example col 12-13) which formulates a target cell array (e.g. 8X9 array of wells in a microtiter dish seeded with cells) prior to DNA transfection in order to locate the cell in a spatially positioned (e.g. address) manner for ease of identification.

In response, the Applicant respectfully traverses the Examiner’s conclusion and offers the following remarks.

In the Lockett reference, the target cells are seeded on a support (e.g. microtiter plate) and transfected with reagents in solution. However, in the Sabatini method, the reagents are immobilized on a support. The Lockett reference (or the Sabatini reference) does not suggest using immobilized reagent (on a reagent support) to transfect immobilized target cells. The use of free reagents in solution will perform much better than the use of immobilized reagents in the Lockett method.

Furthermore, the Lockett reference uses microtiter dishes as target supports. The physical structure of the microtiter dish prohibits its use with the Sabatini method. In the Sabatini method, since the reagents are immobilized on a flat support (e.g. slide), target cells must be immobilized on a flat support in order to make contact with reagents. Cells in a microtiter dish are at the bottoms of the wells and thus when placed together with reagent immobilized on a slide, they cannot make contact with the reagent. Therefore, one of ordinary skill in the art would find it physically impossible to combine the methods of the two references in the manner suggested by the Office Action.

“Alternatively, the Palsson reference teaches a method of promoting transfection efficiency by providing a reagent array... ..The Palsson reference provides for the separation of the reagent array from the target; and the reference examples illustrate the monitoring transfection efficiency through assays requiring the designation and corresponding of array locations spatially for both the reference reagent and target (if immobilized)”.

Applicant respectfully traverses the Examiner’s conclusion. Palsson does not teach the use of target cells immobilized on a support that is different from the reagent support. In the Palsson method (see col. 3-6, col. 7 line 43-55 and examples), DNA particles are immobilized on the cell growth support. The target cells are also directed onto the same cell growth support. Therefore, similar to the Sabatini method, Palsson use one solid cell growth support for both reagents and targets. In contrast, in the method of Claim 37 (and

the dependent claims), reagents are immobilized on an array while target cells are immobilized on a growth support which is different from the reagent array.

The method of Palsson does not teach the separation of the reagent from the target. In the method, particles (DNA) are loaded onto a cell growth support and the target cells are contacted with the particle-loaded growth support (col. 3). Therefore, the target cells and DNA particles are on the same support and cannot be separated. The method of Claim 53 further comprises the step of separating said target support from said array. The method cannot be anticipated by Sabatini in view of Palsson.

Therefore, neither Palsson nor Lockett teaches or suggests the separation of target from array. The method of Claim 53 is not obvious to one of ordinary skill in the art.

The examiner further states that “accordingly, the Lockett and Palsson reference taken separately or in combination provide motivation to one of ordinary skill in the art to modify the Sabatini method by utilizing a target support in order to a. specially address the target for improved identification (e.g. with the reagent) as taught by Lockett; and/or b. to improve transfection efficiency as taught by Palsson”.

“Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant’s invention to modify the Sabatini reference to utilize a target attached to a support for purpose of improving assay identification and/or promoting transfection efficiency.”

As argued above, both the Palsson and the Lockett methods teach the use of one support for both targets and reagents. Neither method teaches or suggests the use of two separate supports for reagents and targets as in the method of Claim 37.

Furthermore, none of the references teaches or suggests the step of separating target from array, as taught in the method of Claim 53. Therefore, Claims 37 and 53 are patentable over Sabatini in view of Palsson and/or Lockett et al.

In summary, each of the Examiner's objections and rejections has been addressed. And in response to Examiner's Objections and/or Rejections, Applicant has withdrawn Claims 54-56 and has amended Claims 37 and dependent claims

Respectfully submitted,

A handwritten signature in black ink, reading "Yingjian Wang". The signature is written in a cursive, flowing style.

Yingjian Wang

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